Docket No.: 4705-0106PUS1
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Ogari PACHECO et al.

Application No.: Not Yet Assigned

Confirmation No.: N/A

Filed: December 9, 2004

Art Unit: N/A

For: SOLUBLE STABLE PHARMACEUTICAL COMPOSITION FOR THE ADMINISTRATION OF HIV PROTEASE INHIBITORS AND A PROCESS FOR THE PREPARATION OF CONCENTRATED PHARMACEUTICAL COMPOSITIONS FOR THE ADMINISTRATION OF HIV PROTEASE INHIBITORS

Examiner: Not Yet Assigned

LETTER

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The PTO is requested to use the amended sheets/claims attached hereto (which correspond to Article 19 amendments or to claims attached to the International Preliminary Examination Report (Article 34)) during prosecution of the above-identified national phase PCT application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §1.16 or 1.14; particularly, extension of time fees.

Dated: December 9, 2004

Respectfully submitted,

By _____
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Attachment(s)

CLAIMS

1. Pharmaceutical composition characterized by comprehending:

   (a) A therapeutic amount of the protease inhibitor [5S-(5R*,8R*,10R*,11R*)]-10 - hydroxy - 2 - methyl-5-(1-methylethyl)-1-[2-(1-methylethyl)- 4 - thiazolyl] - 3,6 - dioxo - 8,11 - bis (phenylmethyl) - 2,4,7,12-tetraazatridecan-13-oic acid 5-thiazolylmethyl ester (ritonavir);

   (b) A mixture of alcoholic solvent and alcoholic co-solvent from C_2-C_4;

   (c) A mixture of medium chain mono/diglycerides of C_8-C_{10};

   (d) A pharmaceutical suitable surfactant;

   (e) An antioxidant.

2. Pharmaceutical composition accordingly with claim 1, characterized by optionally comprehend:

   (a1) An emulsion stabilizer;

   (b1) A polarity corrector.

3. Pharmaceutical composition in accordance with claim 1, characterized by employing the protease inhibitor [5S-(5R*,8R*,10R*,11R*)]-10 - hydroxy - 2 - methyl-5-(1-methylethyl)-1-[2-(1-methylethyl)- 4 - thiazolyl] - 3,6 - dioxo - 8,11 - bis (phenylmethyl) - 2,4,7,12-tetraazatridecan-13-oic acid 5-thiazolylmethyl ester (ritonavir) in a concentration from 1.0% to 60% in weight of the final composition, more preferably in a concentration from 10% to 50% in weight of the final composition;

4. Pharmaceutical composition in accordance with claim 1, characterized by the alcoholic solvent is used in a

concentration from 5.0% to 20% in weight of the final composition, more preferably in a concentration from 5.0% to 15% in weight of the final composition;

5. Pharmaceutical composition in accordance with claim 1, characterized by the alcoholic co-solvent is used in a concentration from 5.0% to 20% in weight of the final composition, more preferably in a concentration from 5.0% to 15% in weight of the final composition;

6. Pharmaceutical composition in accordance with claim 1, characterized by the alcoholic solvent and the alcoholic co-solvent are used in a concentration from 10% to 40% in weight of the final composition, more preferably in a concentration from 10% to 30% in weight of the final composition;

7. Pharmaceutical composition in accordance with claim 1, characterized by the medium chain mono/diglycerides mixture of C_8-C_{10} is used in a concentration from 20% to 80% in weight of the final composition, more preferably in a concentration from 20% to 70% in weight of the final composition.

8. Pharmaceutical composition in accordance with claim 1, characterized by the surfactant is used in a concentration from 0.1% to 20% in weight of the final composition;

9. Pharmaceutical composition in accordance with claim 1, characterized by the antioxidant is used in a concentration from 0.001% to 2.0% in weight of the final composition;

10. Pharmaceutical composition in accordance with claim 1, characterized by the alcoholic solvent is ethanol and the alcoholic co-solvent is propylene glycol;

Replaced by art 19

11. Pharmaceutical composition in accordance with claim 1, characterized by the surfactant is polyethoxylated castor oil 35, and/or hydrogenated polyethoxylated castor oil 40, and/or polysorbates 20, 40, 60 or 80;

12. Pharmaceutical composition in accordance with claim 1, characterized by the antioxidant is butylated hydroxy toluene and/or alpha-tocopherol;

13. Pharmaceutical composition in accordance with claim 1 or 2, characterized by employing an emulsion-stabilizing agent in an concentration from 0% to 60% in weight of the final composition;

14. Pharmaceutical composition in accordance with claim 1 or 2, characterized by the emulsion-stabilizing agent is polyethylene glycol 400 (PEG 400);

15. Pharmaceutical composition in accordance with claim 1 or 2, characterized by employing a polarity corrector agent in a concentration from 0% to 0.5% in weight of the final composition;

16. Pharmaceutical composition in accordance with claim 1 or 2, characterized by the polarity corrector agent is citric acid and/or ascorbic acid;

17. Pharmaceutical composition in accordance with claims 1 to 16, characterized by the being used for oral administration as an oral solution, hard gelatin capsules and/or soft gelatin capsules;

18. Pharmaceutical composition in accordance with claims 1 to 16, characterized by being preferably employed for oral administration as soft gelatin capsules;

19. Pharmaceutical composition in accordance with claims 1 to 16, characterized by being employed in the treatment of viral infections;

Replaced by Art 19

20. Pharmaceutical composition in accordance with one of the claims 1 to 16, characterized by being employed in medicine or veterinary;

21. Process for preparation of soluble concentrate pharmaceutical compositions of [5S-(5R*,8R*,10R*,11R*)]-10 - hydroxy - 2 - methyl-5-(1-methylethyl)-1-[2-(1-methylethyl)- 4 - thyazolyl] - 3,6 - dioxo - 8,11 - bis (phenylmethyl) - 2,4,7,12-tetraazatridecan-13-oic acid 5-thiazolylmethyl ester (ritonavir), characterized by comprehend the following steps:

(a2) Completely dissolution of [5S-(5R*,8R*,10R*,11R*)]-10 - hydroxy - 2 - methyl-5-(1-methylethyl)-1-[2-(1-methylethyl)- 4 - thiazolyl] - 3,6 - dioxo - 8,11 - bis (phenylmethyl) - 2,4,7,12-tetraazatridecan-13-oic acid 5-thiazolylmethyl ester (ritonavir), in a sufficient amount of the alcoholic solvent C_2-C_4, under controlled temperature;

(b2) Elimination of solid particles by means of filtration;

(c2) Evaporation the alcoholic solvent, under reduced pressure at low temperatures to about half the initial concentration;

(d2) Addition the alcoholic co-solvent, the medium chains mono/diglycerides mixture, the antioxidant, the emulsion-stabilizing agent and the polarity corrector in the appropriate amounts for the composition;

(e2) Removing the alcoholic solvent by distilling under reduced pressure until the remaining quantity is the desired quantity in the composition;

Replaced by Art 19

(f2) Adding the surfactant under continuous stirring and maintain stirring until mixture is complete.

(g2) Correct the composition final weight by the addition of the alcoholic solvent employed in the initial dissolution of ritonavir, if necessary.

22. Process for preparation of soluble concentrate pharmaceutical compositions accordingly with claim 21, characterized by the alcoholic solvent used in (a2) is ethanol;

23. Process for preparation of soluble concentrate pharmaceutical compositions accordingly with claim 21, characterized by the dissolution described in (a2) is conducted in a temperature from 30°C to 45°C;

24. Process for preparation of soluble concentrate pharmaceutical compositions accordingly with claim 21, characterized by the evaporation of the alcoholic solvent under reduced pressure is conducted at a maximum temperature of 40°C;

25. Process for preparation of soluble concentrate pharmaceutical compositions accordingly with claim 21, characterized by the co-solvent being propylene glycol;

26. Process for preparation of soluble concentrate pharmaceutical compositions accordingly with claim 21, characterized by the medium chain mono/diglycerides mixture is a mixture of medium chain mono/diglycerides of C_8-C_{10};

27. Process for preparation of soluble concentrate pharmaceutical compositions accordingly with claim 21, characterized by the antioxidant is butylated hydroxy toluene or alpha-tocopherol;

Replaced by A19

28. Process for preparation of soluble concentrate pharmaceutical compositions accordingly with claim 21, characterized by the emulsion stabilizing agent is polyethylene glycol 400 (PEG 400);

29. Process for preparation of soluble concentrate pharmaceutical compositions accordingly with claim 21, characterized by the polarity corrector is citric acid or ascorbic acid;

30. Process for preparation of soluble concentrate pharmaceutical compositions accordingly with claim 21, characterized by the surfactant is polyethoxylated castor oil 35, and/or polyethoxylated hydrogenated castor oil 40, and/or polysorbates 20, 40, 60 or 80;

31. Process for preparation of soluble concentrates pharmaceutical compositions accordingly with claim 21, characterized by being employed in the preparation of concentrated pharmaceutical compositions of ritonavir for oral administration.

Replaced by Art 19